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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/646,939 | 11/14/2000 | Conor Mulrooney | 7146-106 | 1308 |

7590 05/18/2004

Thomas Q Henry
Woodard Emhardt Naughton Moriarty & McNett
111 Monument Circle Suite 3700
Bank One Tower
Indianapolis, IN 64204

| EXAMINER | |
|---|---|
| CHUNDURU, SURYAPRABHA | |
| ART UNIT | PAPER NUMBER |
| 1637 | |

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/646,939 | MULROONEY, CONOR | |
| | Examiner | Art Unit | |
| | Suryaprabha Chunduru | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18 and 20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicants' response to the office action and amendment filed on February 3, 2004, has been entered.

2. Claims 1, 20-23 are amended. Claims 1-18, and 20-26 are pending.

3. This application is a 371 of PCT/GB99/00929 filed on March 24, 1999.

### *New Rejections*

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18, 20-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Clams 1 and 20 recite in step (b) "degree of sequence homology", which is unclear and indefinite because it is not clear to to what extent the degree of homology means, is it a one base homology with the first and second primers or a two base or 3 base sequence homology or so on.

### *Claim Rejections - 35 USC § 102*

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following rejection is based on the broadest claim interpretation, specifically for the claim limitations as "a digestion resistant region" and "enzyme having 5'-double

strand specific exonuclease activity and enzyme having strand displacing polymerase activity".

Claims 1-9, 13-18, 20-26 rejected under 35 U.S.C. 102(b) as being anticipated by Walker et al. (USPN. 5,270,184) ('184).

Walker et al. ('184) teach an isothermal method of clams 1, 7-8, 13-17, 20-26 of amplification of a target nucleic acid (RNA and /or DNA) wherein ('184) disclose that the method comprises

(a) hybridizing a first and second primer with first and second complementary nucleic acid fragments, with binding region at 3'-ends of the said target nucleic acid fragments and includes at its 5'-end a digestion resistant region (hemiphosphothiorate HincII recognition site) which allows partial digestion of the primer by the enzyme having 5'-double strand specific exonuclease activity Klenow or Bst or Bca DNA polymerase enzymes display 5'-double strand specific exonuclease activity at a nick site (see column 11, lines 1-16, and 30-61);

(b) third and fourth primers having a degree of sequence homology (complementary) with first and second primers and bind at their 3'- ends (column 11, lines 37-43);

(c) providing an enzyme having strand displacing polymerase activity and enzyme having 5'-double strand specific exonuclease activity (exo$^-$ klenow DNA polymerase, Bst, or Bca) (see column 11, lines 1-15, lines 30-61) and

(e) dNTPs, under conditions allowing hybridization, strand displacement polymerization thereby producing an amplified amount of the first and second strands (see column 11, lines 44-61);

With regard to clams 2, 18, Walker et al. ('184) also disclose that the method also comprises target nucleic acid from a single or double stranded DNA or RNA or complementary DNA generated from RNA (single stranded) (see column 4, lines 46-51);

With regard to clams 3-4, Walker et al. ('184) also disclose that the method comprises modified nucleotides (phosphothiate linkage) (see column 11, lines 44-45);

With regard to clams 5-6, 9, Walker et al. ('184) also disclose that first and second primers comprise a length between 30 and 100 nucleotides, and third and fourth primers comprise a length ranging between 5 and 50 bases or nucleotides (see column 8, lines 28-31);

With regard to clams 11, Walker et al. ('184) also disclose that the strand displacing DNA polymerase is selected from Klenow DNA polymerase, sequenase, Bst DNA polymerase, Phi29 DNA polymerase, T5 DNA polymerase (see column11, lines 1-16);

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walker et al. (USPN. 5,270,184) and in view of Walker et al. (EP 0 500 224).

Walker et al. ('184) teach an isothermal method of amplification of a target nucleic acid (RNA and /or DNA) wherein ('184) disclose that the method comprises

(a) hybridizing a first and second primer with first and second complementary nucleic acid fragments, with binding region at 3'-ends of the said target nucleic acid fragments (see column 11, lines 30-37);

(b) third and fourth primers having a degree of sequence homology with first and second primers and bind at their 3'- ends (column 11, lines37-43);

(c) providing an enzyme having strand displacing polymerase activity (exo$^-$ klenow DNA polymerase) and

(e) dNTPs, under conditions allowing hybridization, strand displacement polymerization thereby producing an amplified amount of the first and second strands (see column 11, lines 44-61);

Walker et al. ('184) also disclose that the strand displacing DNA polymerase is selected from Klenow DNA polymerase, sequenase, Bst DNA polymerase, Phi29 DNA polymerase, T5 DNA polymerase (see column11, lines 1-16); However, Walker et al. ('184) did not specifically teach the enzyme having 5'-double strand specific exonuclease activity is T7 Gene 6 exonuclase.

Walker et al. ('224) teach a method for amplifying complementary first and second nucleic acid sequences each having a binding region at its 3' end wherein the method comprises (a) treating single stranded nucleic acid sequences with one or more primers (see column 10, lines 40-53) (in case of two primers, first primer hybridizes with first strand and the second primer hybridizes with the second strand (see column 7, lines 18-25); (c and d) in the presence of a double strand specific exonuclease (see column 10, lines 40-53) and (e) modified deoxynucleoside triphosphates (dNTPs), allowing the reaction to proceed for a period of time sufficient to generate amplified reaction products

(see column 10, lines 46-57). Wlaker et al. ('224) also disclose that (a) the modified or substituted dNTPS incorporated during amplification are resistant to digestion (see column 8, lines 36-43); (b) exonuclease used was T7 gene 6 exonuclease (see column 8, lines 29-53, column 11, lines 45-46); other exonucleases and polymerases useful for the method include lamda exonuclease, klenow fragment of DNA polymerase I and Bst polymerase (see column 8, lines 51-53, and column 9 lines 1-6); the primer length could be 15-100 nucleotides (see column 8, lines 15-16).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of amplification of single stranded nucleic acid sequences as taught by Walker et al. ('184) with the method as taught by Walker et al. ('224) because Walker et al. ('224) taught that "the use of exonuclease in combination with polymerase, which can digest double-stranded DNA which does not comprise digestion resistant region (see column 8, lines 29-53). An ordinary practitioner would have been motivated to combine the method of Walker et al. ('184) with the method of Walker et al. ('224) in order to achieve the expected advantage of a rapid and sensitive method for detecting a multiple complementary target sequences since incorporation of exonuclease, in addition to a DNA polymerase, could digest the nonspecifically amplified double stranded DNA and would reduce the background noise and improve the sensitivity of detection of many unknown complementary target nucleic acids.

***Response to Arguments***

7. Applicant's response to the office action is fully considered and found persuasive.

8. The rejection made under 35 U.S.C. 112 second paragraph in the previous office action is withdrawn herein in view of the applicants' amendment.

9. With reference to the rejection made in the previous office action under 103(a), Applicants' arguments and amendment are fully considered and the rejection is with drawn in view of the arguments and new grounds of rejection.

***Conclusion***

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
May 12, 2004

JEFFREY FREDMAN
PRIMARY EXAMINER